

ANALYSIS OF THE FREQUENCY OF ENDOMETRIAL CANCER RECURRENCE IN STAGE I-II.

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Introduction

An increase in the incidence of endometrial cancer requires not only early detection of this disease, but also appropriate treatment, taking into account clinical, morphological, molecular-genetic prognostic factors and the frequency of recurrences (fig.1,2).

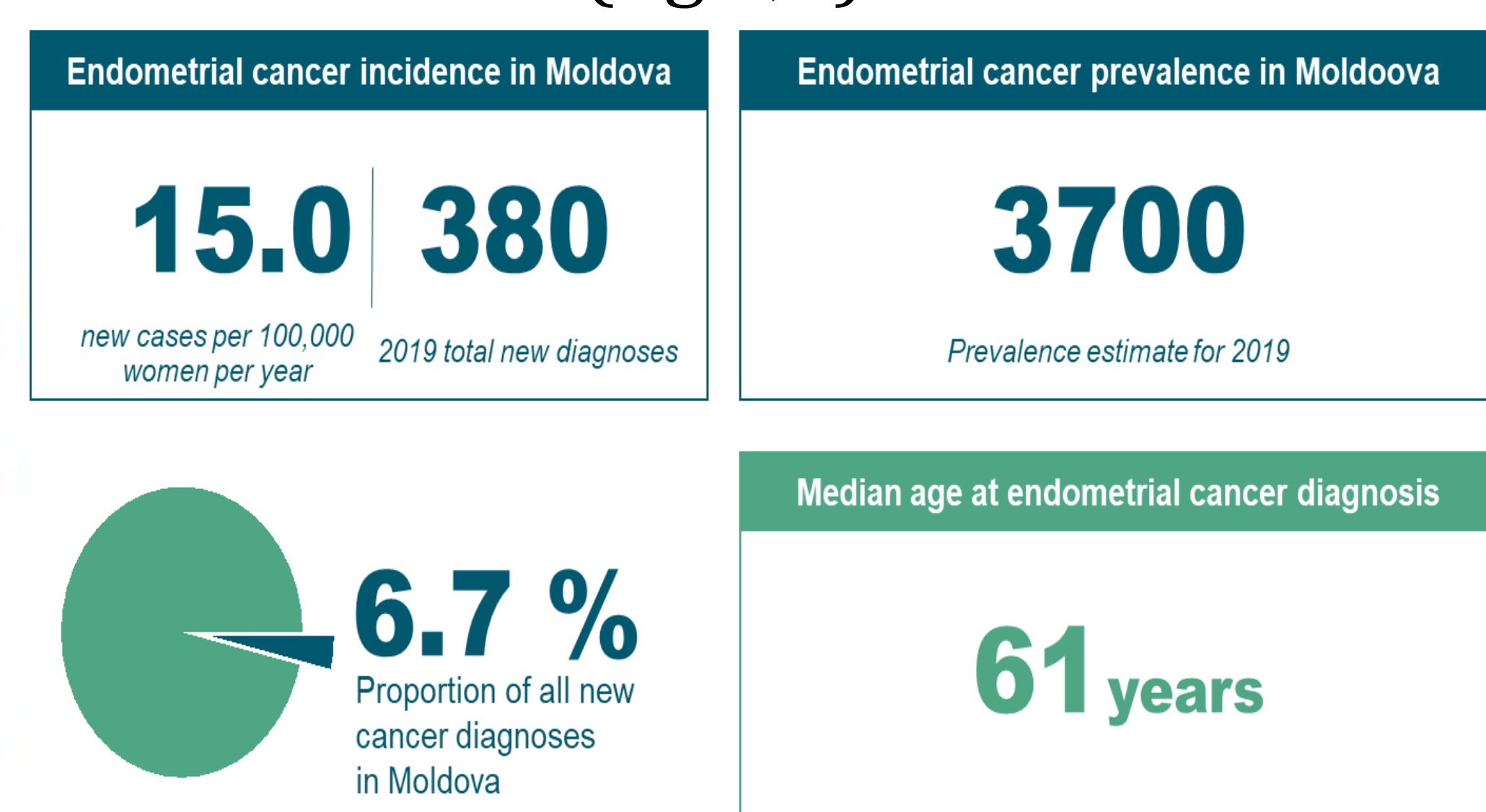


Fig. 1 Incidence of endometrial cancer in Moldova

Keywords

endometrial cancer, frequency of recurrence, surgical treatment, clinical factors, morphological factors, molecular factors, cell proliferation, Ki-67

Purpose

The aim of this study was to study the morphological factors of the prognosis and the characteristics of endometrial cancer recurrence in stage I-II, with the introduction of a classification based on the molecular characteristics of tumors.

Material and methods

The study represents a complex, prospective analysis of clinical-morphological data and recurrence rates in 200 patients with stage I-II who were treated at the Department of Gynecological Oncology of the Institute of Oncology of the Republic of Moldova for 2015-2018, based on ESGO risk criteria (fig.3).

	Clinical	Molecular	Pathological
Prognostic Factors Positive	<ul style="list-style-type: none"> ≤40 years at diagnosis American Indian/ Alaska native Metformin use 	<ul style="list-style-type: none"> Hormone receptor-positive MSI-positive POLE-ultramutated (TCGA classification) Activating KRAS mutation 	<ul style="list-style-type: none"> Type I histologic subtype Early FIGO stage Low histologic grade
Prognostic Factors Negative	<ul style="list-style-type: none"> >40 years at diagnosis Black Obesity Nulliparity 	<ul style="list-style-type: none"> Hormone receptor-negative Loss-of-function TP53 mutation HER2 amplification Upregulation of angiogenesis markers (high microvascular proliferation) LCAM1-positive⁵ High copy number (TCGA classification)² P13K/AKT/mTOR pathway activation 	<ul style="list-style-type: none"> Type II histologic subtype Advanced FIGO stage High histologic grade Presence of lymphovascular space invasion Deep myometrial invasion

Fig. 2 Clinical, pathological, molecular factors influence prognosis of EC

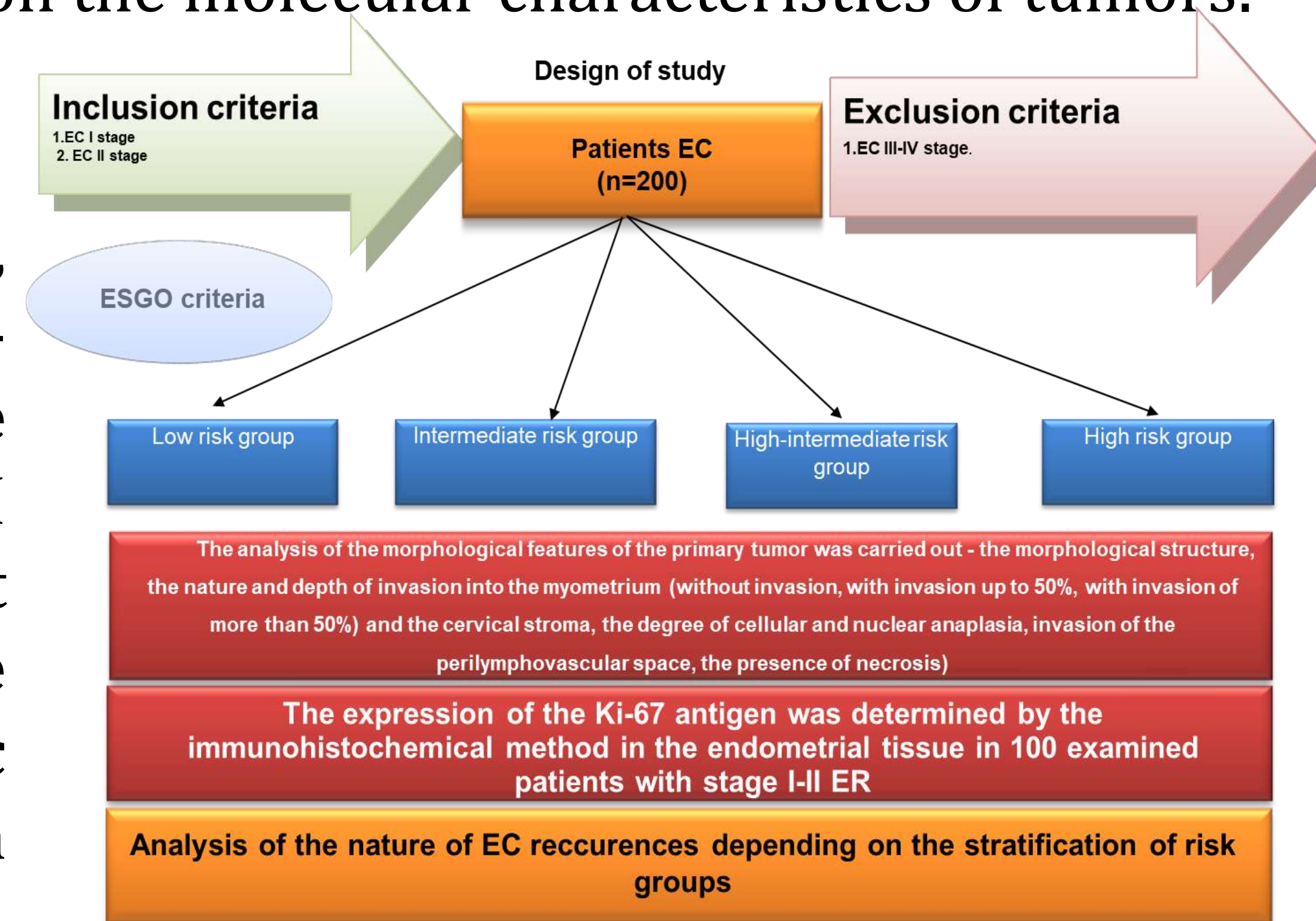


Fig. 3 Design of study

Results

Free interval before recurrence was 24 months. In 11 patients, recurrence developed up to 24 months and in 9 to 60 months. An indicator of the aggressiveness of the tumor process is cell proliferation, which can be assessed using the percentage of Ki-67 positive nuclei(fig.5). A high percentage of Ki-67 is associated with an unfavorable prognosis of the EC. When analyzing the expression index Ki-67, it was found that in the low-risk group of patients with EC, the Ki-67 index was 14%, from the group with intermediate risk, the expression level was 25.5%, from the high risk group(fig.4).

the degree of tumor differentiation in patients with endometrial cancer	Level Ki-67<49%		Level Ki-67>49%	
	n	%	n	%
High (n=24)	20	83	4	17
Intermediate (n=50)	30	60	20	40
Low (n=26)	8	30	18	70

Fig. 4 Dependence of the Ki-67 index expression on the degree of tumor differentiation in patients with endometrial cancer

Conclusions

In the first three years of observation, recurrences of the underlying disease were observed in the general group of patients examined with EC in stage I-II. Of the 200 patients with stage I-II, recurrences and metastases were detected in 20 (40%) patients. Clarification of the risk group during the initial examination and immediately after the surgical treatment of patients with endometrial cancer using clinical, morphological and immunohistochemical methods and our results make it reasonable to monitor EC at early stages even in the low-risk group and to search for new molecular genetic prognostic factors.

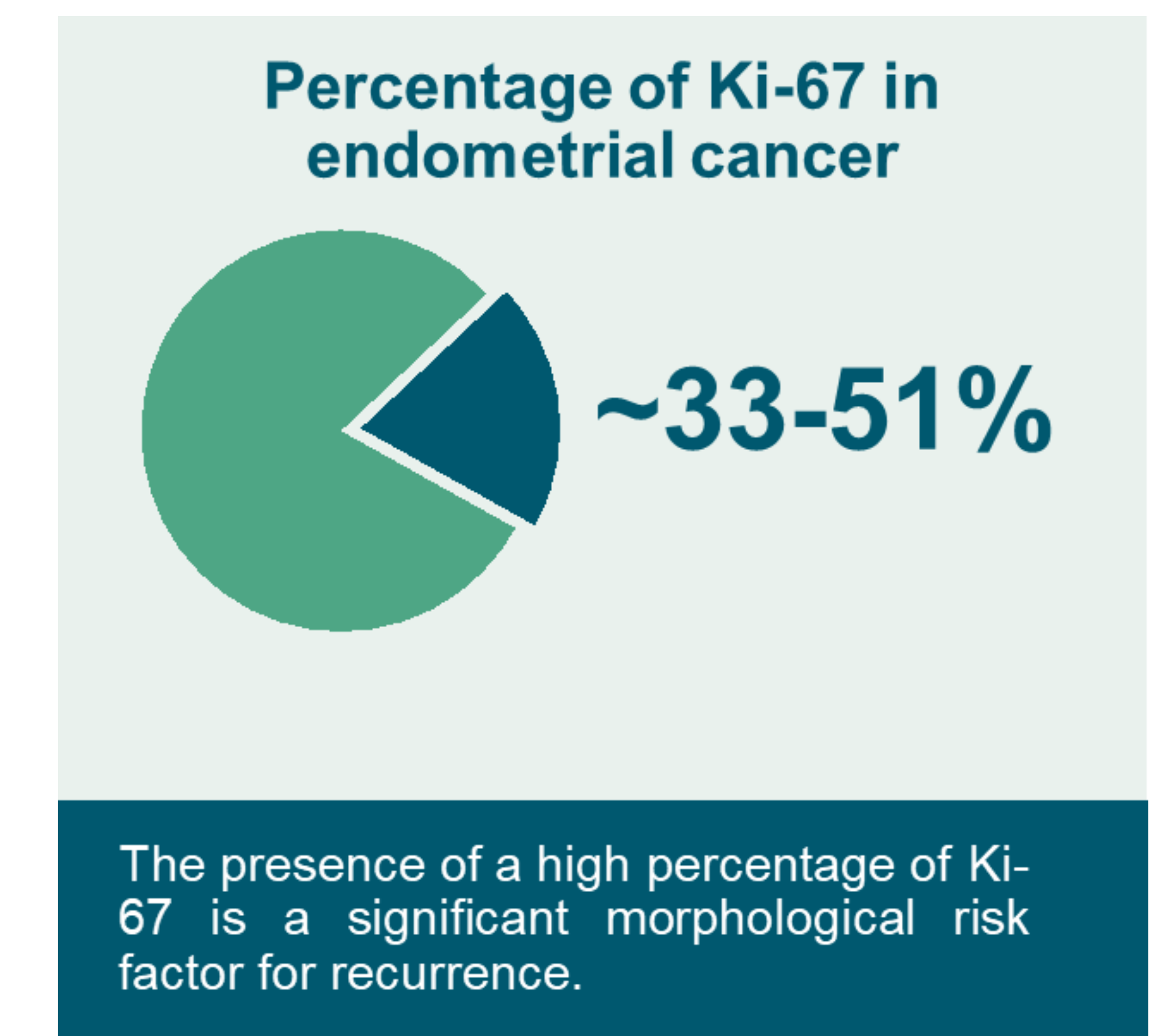


Fig. 5 Percentage of Ki-67 in EC